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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/563,570 | 08/25/2006 | David H. Wagner | 059742-5001 | 1193 |

9629 7590 08/28/2007

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| EXAMINER | |
|---|---|
| COOK, LISA V | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 08/28/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/563,570 | WAGNER, DAVID H. | |
| | Examiner | Art Unit | |
| | Lisa V. Cook | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *9-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 27* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☒ Claim(s) *1-27* are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 January 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/6/06 & 7/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group I (claims 1-8 and 27) in the reply filed on 7/23/07 is acknowledged. The traversal is on the ground(s) that Wagner et al. does not teach that the level of $CD40^+$ T-cells is predictive of type I diabetes. This is not found persuasive because Wagner et al. disclose that $CD4^+CD40^+$ cells infiltrate the pancreatic islets causing β-cell de-granulation and ultimate diabetes. See abstract. It was also demonstrated that $CD4^{lo}CD40^{hi}$ T-cells induced diabetes. See page 3786 and figure 6.

2. Further, the inventions listed as Groups A through C in the paper mailed 6/21/07, do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Under PCT rules Applicant is entitled to an examination of one of the combination groupings: (1) a product, a method of using said product and a method of producing said product. The instant claims are directed to multiple methods. Accordingly, Applicant must select one for further prosecution.

3. The requirement is still deemed proper and is therefore made FINAL.

4. Claims 9-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/23/07.

***Priority***

5. If applicant desires priority under 35 U.S.C. 120 to application number PCT/US04/21646 filed July 7, 2004 based upon previously filed applications, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression *"now Patent No. _____" should follow the filing date of the parent application.* If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii).

This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c).

The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

6. The instant application should be updated to include application number PCT/US04/21646 filed July 7, 2004. Please include "371 of PCT/US04/21646 filed July 7, 2004", to the specification.

### *Information Disclosure Statement*

7. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 lists the references, they have not been considered.

8. The information disclosure statement filed 1/6/07 has been considered as to the merits prior to First Action.

9. The information disclosure statement filed 7/23/07 has been considered as to the merits before First Action.

### *Drawings*

10. The drawings are objected to under 37 CFR 1.83(a) because they fail to show panels 7A, 7B, 8A, and 8B as described in the specification. Please label panels A and B for figures 7 and 8. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended.

The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

***Specification***

11. The use of the trademarks has been noted in this application. For example see, FICOLL on page 34. They should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

***Abstract***

12. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

### *Claim Objections*

13. Claim 3 is objected to because of the following informalities: Claim 3 utilizes acronyms (see for example Il, IL, TGF, IFN, etc). Although the terms may have art-recognized meanings, it is not clear if applicant intends to claim any prior art definition of the abbreviations. The terms should be defined in their first instance. The initial explanation will convey intended meaning of subsequent abbreviations in the claims (IL is interleukin). Please define in the claims in order to obviate this objection.

### *Claim Rejections - 35 USC § 102*

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**I.** Claims 1, 4, 7, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Berner et al. (Ann Rheum Dis, 2000, Vol.59, pages 190-195).

Berner et al. disclose that CD40L-CD40 interactions are involved in humoral and numerous cell mediated responses. See abstract and page 190 2nd column. The researchers employ antibody staining and flow cytometry procedures to detect $CD4^{+}CD40L^{+}$ T cells. See page 191– 2nd column and figure 1, for example. Heparinised peripheral blood samples of 62 patients with rheumatoid arthritis (RA) and 20 healthy controls were tested. See page 191-Methods. CD40L expression correlated with increased disease activity and this correlation was higher in the RA $CD40L^{high+}$ group than in the $CD40L^{low+}$ group. See page 194, 2nd column, last paragraph.

Although Berner et al. recite the measurement of $CD4^+CD40L^+$ T cells, this is deemed the same composition claimed ($Cd^{lo}CD40^{hi}$) because the specification teaches that Cd4+CD40+ refers to low levels of CD4 and high levels of CD40 and is the same cell population as CD4loCD40+. See specification page 9 lines 30-33, for example.

**II.** Claims 1, 4, 5, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al. (PNAS, March 19, 2002, Vol.99, No.6, pages 3782-3787).

Wagner et al. disclose antibody staining and flow cytometry procedures to detect $CD4^+CD40^+$ T cells. See page 3782 – 2nd column. T cells were isolated from spleen, thymus, or pancreas of diabetic NOD (nonobese diabetic) mice. The NOD mouse has been used extensively as a model for human type 1 autoimmune diabetes. See page 3782 1st column 3rd paragraph. The cells were triple stained with phycoerytherin vs. directly conjugated anti-CD4 and FITC-conjugated anti-CD40.

The researcher found that CD40 is functionally expressed on CD4+ T cells and may have an important role in the pathogenesis of autoimmune diseases. See page 3783 1st column – Results. The data suggested that $CD40^{lo}CD4^{hi}$ T cells were 32% in the periphery of spleen. Whereas only 7% of the T cells from BALB/control mice were $CD4^{lo}CD40^{hi}$. See page 3786 1st column and page 3787. The diabetogenic T cell clones expressed CD40 while the nondiabetogenic T cell clones (controls) were $Cd40^-$. See page 3783 – Results and figure 1.

## *Claim Rejections - 35 USC § 103*

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102((e), f) or (g) prior art under 35 U.S.C. 103(a).

**III.** Claims 2, 3 and 6 are rejected under 35 U.S.C. 103(b) as being unpatentable over Berner et al. (Ann Rheum Dis, 2000, Vol.59, pages 190-195) or Wagner et al. (PNAS, March 19, 2002, Vol.99, No.6, pages 3782-3787) in view of Jeffery PK (Novartis Foundation Symposium, 2001, Vol.234, page 149-161, Abstract Only) and Wald et al. (FASEB, 2003, 17(7), page C177, Abstract).

Please see Berner et al. and Wagner et al. as set forth above.

Berner et al. and Wagner et al. differ from the instant invention in not specifically teaching the measurement of emphysema and at least one cytokine.

However, Jeffery PK teaches that cytotoxic T lymphocytes CD8 are involved in emphysema and asthma is a helper T cell CD4 type inflammatory disorder. However, there may be important similarities and overlap, particularly in more severe asthma. Gene expression for IL-4 and IL-5 were seen in the disorders and it is speculated that the CD4/CD8 T lymphocyte ratio is relevant and important to the development of COPDs. See abstract.

Although Jeffery PK is silent with respect to $CD4^+CD40^+$ cells, Wald et al. teaches that $CD4^+CD40^+$ T cells are involved in the progression of asthma. Further, these cells produce IL-2, IFNγ, IL-4, and IL-10. See abstract.

Therefore, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to utilize the immunoassay measurements of $CD4^+CD40^+$ cells as taught by Berner et al. and Wagner et al. to measure emphysema and cytokine expression as taught by Jeffery and Wald et al. because Jeffrey PK taught that CD4 is involved in the development of COPDS (emphysema/asthma) and the disorders may have similarities and overlap, while Wald et al. taught that $CD4^+CD40^+$ T cells are involved in the progression of asthma. Further these cells produce IL-2, IFNγ, IL-4, and IL-10. See abstract.

One of ordinary skill in the art would have been motivated to do this in order to evaluate COPDs for evaluation and treatment.

**IV.** Claim 27 is rejected under 35 U.S.C.103 (a) as being unpatentable over Berner et al. (Ann Rheum Dis, 2000, Vol.59, pages 190-195) or Wagner et al. (PNAS, March 19, 2002, Vol.99, No.6, pages 3782-3787) in view of Foster et al. (U.S. Patent #4,444,879).

Please see Berner et al. and Wagner et al. as set forth above.

Although Berner et al. and Wagner et al. teach the reagents required by the claims; they do not specifically teach the reagents in kit configurations.

In other words, the reference fails to teach the reagents as a kit. However, kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example. In their patent kits including the reactant reagents, a microplate, positive controls, negative controls, standards, and instructions are taught. The reagents are compartmentalized or packaged separately for utility. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay reagents as taught by Berner et al. or Wagner et al. and format them into a kit because Foster et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay. Kits are also economically beneficial in reagent distribution.

***Double Patenting***

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**V.** Claims 1, 4, 5, 7, 8, and 27 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 11/399,384. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the measurement of the same cells. The instant invention recites the measurement of $CD4^{lo}CD40^{hi}$ T cells, while application number 11/399,384 recited $CD^{+}CD40^{+}$T cells. Both disclosures teach that these cells are the same. See page 18 section 0058 in application number 11/399,384 and page 9 lines 30-33 in application number 10/563,570. The terms are taught to be interchangeable. Accordingly, the methods are not patentably distinct from each other. The claims of application number 11/399,384, encompasses the instantly claimed invention. Accordingly, the methods are not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**VI.** Claims 2, 3, and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 11/399,384 in view of Jeffery PK (Novartis Foundation Symposium, 2001, Vol.234, page 149-161, Abstract Only) and Wald et al. (FASEB, 2003, 17(7), page C177, Abstract).

Please see Application No. 11/399,384 as set forth above.

Application No. 11/399,384 differs from the instant invention in not specifically teaching the measurement of emphysema and at least one cytokine.

However, Jeffery PK teaches that cytotoxic T lymphocytes CD8 are involved in emphysema and asthma is a helper T cell CD4 type inflammatory disorder. However, there may be important similarities and overlap, particularly in more severe asthma. Gene expression for IL-4 and IL-5 were seen in the disorders and it is speculated that the CD4/CD8 T lymphocyte ratio is relevant and important to the development of COPDs. See abstract.

Although Jeffery PK is silent with respect to $CD4^+CD40^+$ cells, Wald et al. teaches that $CD4^+CD40^+$ T cells are involved in the progression of asthma. Further, these cells produce IL-2, IFNγ, IL-4, and IL-10. See abstract.

Therefore, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to utilize the immunoassay measurements of $CD4^+CD40^+$ cells as taught Application No. 11/399,384 to measure emphysema and cytokine expression as taught by Jeffery and Wald et al. because Jeffrey PK taught that CD4 is involved in the development of COPDS (emphysema/asthma) and the disorders may have similarities and overlap, while Wald et al. taught that $CD4^+CD40^+$ T cells are involved in the progression of asthma. Further these cells produce IL-2, IFNγ, IL-4, and IL-10. See abstract.

One of ordinary skill in the art would have been motivated to do this in order to evaluate COPDs for evaluation and treatment. This is a provisional obviousness-type double patenting rejection.

17. For reasons aforementioned and already of record, no claims are allowed.

***Remarks***

18. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Mehling et al. (Critical Reviews in Biochemistry and Molecular Biology, 38(1), pages 1-21, 2/1/03) disclose dendritic cells as regulators of autoimmune responses.

B. Valentini et al. (Journal of Autoimmunity, 2000, Vol.15, pages 61-66) teach the increased expression of CD40 ligand in activated CD4+ cells in sclerosis patients.

19. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 8:30 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lisa V. Cook 8/14/07

*Lisa V. Cook*
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*Art Unit:1641*
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*571-272-0816*
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